## Scheme 1: synthesis of difluorocombretastatin

R<sub>3</sub>

Scheme 2: Synthesis of difluoro-Nitro- and difluoro-Amino-combretastatin

# Scheme 3: Synthesis of monofluorocombretastatins

# Scheme 3a: Total synthesis approach to monofluorocombretastatin

Scheme 4: Synthesis of disodium-phosphate prodrug difluorocombretastatin (ST2493)

Scheme 5: Synthesis of disodium mono-difluorocombretastatin-4-O-methyloxyphosphate [12]

#### FIGURE 6

Scheme 6: General Procedure for obtaining amide derivatives [13].

# Scheme 7: Synthesis of bromofluorocombretastatin